Complete Summary

GUIDELINE TITLE

Anakinra for rheumatoid arthritis.

BIBLIOGRAPHIC SOURCE(S)

National Institute for Clinical Excellence (NICE). Anakinra for rheumatoid arthritis. London (UK): National Institute for Clinical Excellence (NICE); 2003 Nov. 19 p. (Technology appraisal; no. 72).

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Rheumatoid arthritis (RA)

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Treatment

CLINICAL SPECIALTY

Family Practice
Internal Medicine
Rheumatology

INTENDED USERS

Advanced Practice Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To assess the clinical benefits and cost-effectiveness of anakinra for the treatment of adults with rheumatoid arthritis

TARGET POPULATION

Adults with rheumatoid arthritis

INTERVENTIONS AND PRACTICES CONSIDERED

Anakinra (recombinant, nonglycosylated human interleukin-1 [IL-1]-receptor antagonist) (Kineret)

MAJOR OUTCOMES CONSIDERED

- Clinical effectiveness
- Cost-effectiveness

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases
Searches of Unpublished Data

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Clinical Excellence (NICE) commissioned an independent academic centre to perform a systematic literature review on the technology considered in this appraisal and prepare an assessment report. The assessment report for this technology appraisal was prepared by the West Midlands Health Technology Assessment Collaboration (see the "Companion Documents" field).

Search Strategy

The following electronic bibliographic databases were searched with a stop date of 1st November 2002:

Cochrane Library, Medline, Embase, Science Citation Index (SCI), National Research Register (NRR), NHS Database of Reviews of Effectiveness (DARE),

Index to Scientific and Technical Proceedings (ISTP), NHS Economic Evaluation Database (NHS EED), Health Economic Evaluation Database (HEED).

Search terms included the text words: anakinra; kineret; interleukin-1 receptor antagonist; IL- 1ra; rhu-IL-1Ra; and the index terms; arthritis, rheumatoid; receptors, interleukin-1; interleukin-1.

Studies were limited to humans. No language, date or age restrictions were applied. A metasearch engine was used to search the Internet, and links followed up. Proceedings from the American College of Rheumatology and European Congress of Rheumatology meetings were searched electronically for the years 2001 and 2002.

Scrip, Food and Drug Administration (FDA) submissions for new drug applications, European Medicines Agency (EMEA) reports and the pharmaceutical company submission to the National Institute for Clinical Excellence (NICE) were hand searched. The reference lists of identified publications were reviewed to identify any additional studies and/or citations.

Inclusion and Exclusion Criteria

Two reviewers independently applied the following inclusion/exclusion criteria to all potential studies. Disagreements were resolved by discussion, referring to a third party when necessary. Reviewers were not blinded to any features of the report including authorship however inclusion/exclusion decisions were made prior to detailed scrutiny of the results.

Inclusion Criteria

The criteria for inclusion related to the population, intervention and comparator considered and the publication status of the report were applicable to both the clinical effectiveness and cost-effectiveness parts of the review.

Population: Adults aged 18 years and above with rheumatoid arthritis

Intervention: Anakinra (Kineret®) alone or in combination with other drugs

Comparator: Placebo, or other drug treatments for rheumatoid arthritis (RA)

Publication All data to be included irrespective of publication status.

Studies were included in the final analysis of the review if they met the above criteria and the additional criteria for study design and outcomes as specified below for the clinical and cost-effectiveness parts of the review.

Clinical Effectiveness Review

Study design: Randomised or quasi-randomised controlled trials

Outcomes: To include: mortality, morbidity (e.g. disability/mobility, disease progression, joint damage, pain, adverse events), response rates and quality of life.

Cost-Effectiveness Review

Study design: Economic evaluation studies: cost analysis, cost-effectiveness, cost-utility and cost-benefit studies. Existing health economic reviews were also assessed.

Outcomes: To include: quality of life, costs, and incremental cost-effectiveness ratio.

Exclusion Criteria

- Trials only recruiting children with juvenile idiopathic arthritis.
- Trials with no comparator arm.
- Trials which were not randomised. (clinical effectiveness part of review only)
- Articles reporting solely on laboratory measures aimed at investigating disease or treatment mechanisms.

NUMBER OF SOURCE DOCUMENTS

Quantity of Research Available

A total of 1,003 titles and abstracts were retrieved from the literature searches and from screening the reference lists. The Assessment Centre obtained 58 full papers and from these five randomized controlled trials were selected for inclusion in the review.

A flowchart of the results of the search and inclusion/exclusion decisions is provided at Figure 1, and a list of excluded studies is provided in Appendix 6 of the assessment report.

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Meta-Analysis
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Data Synthesis and Analysis

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Clinical Excellence (NICE) commissioned an independent academic centre to perform a systematic literature review on the technology considered in this appraisal and prepare an assessment report. The assessment report for this technology appraisal was prepared by the West Midlands Health Technology Assessment Collaboration (see the "Companion Documents" field).

A detailed tabular summary of the characteristics (i.e., patients, intervention, comparator, and outcomes) and methodological quality of all included studies was undertaken.

Any information specified by companies as "commercial in confidence" was removed from the draft report.

Where appropriate, meta-analysis was undertaken using a fixed effects model.

Data Extraction Strategy

Two reviewers independently extracted data using pre-designed data extraction forms. Disagreements were resolved by discussion. Data from studies with multiple publications were extracted and reported as a single study.

Clinical Effectiveness Review

The following data were extracted:

- Details of the study population and baseline characteristics of the intervention and control groups, with particular reference to disease characteristics and previous treatment history.
- Details of the intervention, such as dose, mode of administration, frequency of administration and duration of treatment
- Details of completion rates across the groups, reasons for withdrawal, loss to follow up.
- Details of individual outcomes measured such as:
    - Changes in disease activity e.g. American College for Rheumatology (ACR) improvement criteria, swollen joint count, pain, joint space narrowing and erosion.
- Changes in quality of life
- Adverse events reported

Results were extracted, where possible for the intention to treat population, as raw numbers, plus any summary measures with standard deviations, confidence intervals and p-values where given.

Cost-Effectiveness Review

The following data were extracted:

- Details of the study characteristics, including type of economic analysis, intervention and comparator, perspective, time frame, modelling used.
- Details of the data used to populate the evaluation and the key assumptions made such as effectiveness data, cost data, health state valuations, discounting rate.
- Details of the results and sensitivity analysis

Quality Assessment Strategy

Two reviewers undertook quality assessments independently, using a structured approach. Disagreements were resolved by discussion, with reference to a third party where necessary.

Clinical Effectiveness Review

The validity of included studies were assessed by looking at the method of randomisation, the concealment of allocation, the comparability of baseline characteristics between the different arms, blinding, withdrawals and losses to follow-up for each patient group. Based on these criteria a Jadad score was calculated. (The Jadad score ranges from 0 to 5, with a score of 5 representing trials of highest quality).

Cost-Effectiveness Review

The criteria of Drummond et al served as an a priori standard for the assessment of economic evaluations. These evaluate the study question, selection of alternatives, form of evaluation, effectiveness data, costs, benefit measurement and valuation, decision modelling, discounting, allowance for uncertainty and presentation of results.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Considerations

Technology appraisal recommendations are based on a review of clinical and economic evidence.

Technology Appraisal Process

The National Institute for Health and Clinical Excellence (NICE) invites 'consultee' and 'commentator' organisations to take part in the appraisal process. Consultee organisations include national groups representing patients and carers, the bodies representing health professionals, and the manufacturers of the technology under review. Consultees are invited to submit evidence during the appraisal and to comment on the appraisal documents.

Commentator organisations include manufacturers of the products with which the technology is being compared, the National Health Service (NHS) Quality Improvement Scotland and research groups working in the area. They can comment on the evidence and other documents but are not asked to submit evidence themselves.

NICE then commissions an independent academic centre to review published evidence on the technology and prepare an 'assessment report'. Consultees and commentators are invited to comment on the report. The assessment report and the comments on it are then drawn together in a document called the evaluation report.

An independent Appraisal Committee then considers the evaluation report. It holds a meeting where it hears direct, spoken evidence from nominated clinical experts, patients, and carers. The Committee uses all the evidence to make its first recommendations, in a document called the 'appraisal consultation document' (ACD). NICE sends all the consultees and commentators a copy of this document and posts it on the NICE website. Further comments are invited from everyone taking part.

When the Committee meets again it considers any comments submitted on the ACD; then it prepares its final recommendations in a document called the 'final appraisal determination' (FAD). This is submitted to NICE for approval.

Consultees have a chance to appeal against the final recommendations in the FAD. If there are no appeals, the final recommendations become the basis of the guidance that NICE issues.

Who is on the Appraisal Committee?

NICE technology appraisal recommendations are prepared by an independent committee. This includes health professionals working in the NHS and people who are familiar with the issues affecting patients and carers. Although the Appraisal Committee seeks the views of organisations representing health professionals, patients, carers, manufacturers and government, its advice is independent of any vested interests.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

No published economic evaluations were found. The Assessment Group developed its own economic model, the Birmingham Rheumatoid Arthritis Model (BRAM), which is a revised version of the model used in the appraisal of etanercept and infliximab. The manufacturer's submission also included an economic analysis of anakinra.

See Section 4.2 of the original guideline document for a detailed discussion of the cost-effectiveness analysis.

The Committee concluded that, although there was evidence of the clinical effectiveness of anakinra in the short term, the extent of the benefit was not sufficient to justify its cost.

METHOD OF GUIDELINE VALIDATION

External Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Consultee organizations from the following groups were invited to comment on the draft scope, assessment report and the appraisal consultation document (ACD). They were also provided with the opportunity to appeal against the Final Appraisal Determination (FAD).

- Manufacturer/sponsors
- Trade organisations
- Professional/specialist and patient/carer groups
- Commentator organisations (without the right of appeal)

In addition, individuals selected from clinical expert and patient advocate nominations from the professional/specialist and patient/carer groups were also invited to comment on the ACD.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

- On the balance of its clinical benefits and cost effectiveness, anakinra is not recommended for the treatment of rheumatoid arthritis, except in the context of a controlled, long-term clinical study.
- Patients currently receiving anakinra for rheumatoid arthritis may suffer loss of well-being if their treatment were discontinued at a time they did not anticipate. Therefore, patients should continue therapy with anakinra until they and their consultant consider it is appropriate to stop.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The recommendations for clinical effectiveness are based on the results of five randomized controlled trials of anakinra.

For cost-effectiveness, the Assessment Group developed its own economic model and considered an economic analysis developed by the manufacturer of anakinra.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate use of anakinra in patients with rheumatoid arthritis

POTENTIAL HARMS

Not stated

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

This guidance represents the view of the Institute, which was arrived at after careful consideration of the available evidence. Health professionals are expected to take it fully into account when exercising their clinical judgement. This guidance does not, however, override the individual responsibility of health professionals to make appropriate decisions in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Implementation and Audit

- Clinicians treating people with active rheumatoid arthritis (RA) should review their current practice in line with the guidance. Anakinra should be used for the treatment of RA only in the context of controlled, long-term clinical studies.
- Local clinical guidelines, protocols or care pathways for the care of people with RA should incorporate the guidance.

IMPLEMENTATION TOOLS

Patient Resources
Quick Reference Guides/Physician Guides

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

National Institute for Clinical Excellence (NICE). Anakinra for rheumatoid arthritis. London (UK): National Institute for Clinical Excellence (NICE); 2003 Nov. 19 p. (Technology appraisal; no. 72).

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2003 Nov

GUIDELINE DEVELOPER(S)

National Institute for Health and Clinical Excellence - National Government Agency [Non-U.S.]

SOURCE(S) OF FUNDING

National Institute for Health and Clinical Excellence (NICE)

GUIDELINE COMMITTEE

Appraisal Committee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) format from the National Institute for Health and Clinical Excellence (NICE) Web site.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Anakinra for rheumatoid arthritis. Quick reference guide. London (UK): National Institute for Health and Clinical Excellence (NICE); 2003 Nov. 2 p. (Technology appraisal 72). Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site.
- The clinical and cost-effectiveness of anakinra for the treatment of rheumatoid arthritis in adults. Assessment report. West Midlands Health Technology Assessment Collaboration; 2003 Dec. 117 p. Available in Portable Document Format (PDF) from the NICE Web site.

Print copies: Available from the National Health Service (NHS) Response Line 0870 1555 455. ref: N0369. 11 Strand, London, WC2N 5HR.

PATIENT RESOURCES

The following is available:

- Anakinra for rheumatoid arthritis. Understanding NICE guidance - information for people with rheumatoid arthritis, their families and carers, and the public. London (UK): National Institute for Health and Clinical Excellence (NICE); 2003 Nov. 8 p. (Technology appraisal 72).

Electronic copies: Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site.

Print copies: Available from the Department of Health Publications Order Line 0870 1555 455. ref: N0370. 11 Strand, London, WC2N 5HR.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC STATUS

This NGC summary was completed by ECRI on March 8, 2006.

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